

Applicant: Christos J. Petropoulos
Serial No.: 09/874,475
Filed: June 4, 2001
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Please amend the subject application as follows:

In the Specification

Please amend the specification by deleting the reference to Figure 10, Figure 11, Figure 12 and Figure 13 on page 11, lines 6-12.

Please also amend the specification by deleting the paragraph on page 59, lines 7-20 and inserting the following paragraph:

A. In one embodiment, drug resistance mutations were introduced into well-characterized X4 tropic (NL4-3) and R5 tropic (JRCSF) viruses. T20 susceptibility was measured using the virus entry assay (**Figure 7**). The fold change (FC) in T-20 susceptibility for each virus was determined by dividing the IC₅₀ of the test virus by the IC₅₀ of the HXB2 strain of HIV- 1. T-20 sensitivity of similar mutant viruses has been reported in the scientific literature (Rimsky et al.,). In this embodiment, viruses with one mutation within the GIV motif of gp41 (DIV, GIM, SIV) were less susceptible to T20 than the wildtype virus (GIV) (**Table 6**). Viruses with two mutations within the GIV motif (DIM, SIM, DTV) were less susceptible to T20 than viruses with one, or no mutations in the GIV motif (**Table 6**).

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Please amend the specification by deleting the paragraph on page 59, lines 22-32 to page 60, lines 1-5, and inserting the following paragraph:

In another embodiment, mutations that may confer reduced (or increased) susceptibility to the entry inhibitor are identified by sequencing the envelope genes of the sensitive and resistant viruses. The deduced amino acid sequences of the sensitive and resistant viruses are compared to identify candidate drug resistance mutations. The ability of a specific mutation to confer altered drug susceptibility is confirmed or disproved by introducing the mutation into a drug sensitive virus and measuring the susceptibility of the mutant virus in the virus entry assay. In the example represented here, a short stretch of amino acid sequences within the first heptad repeat (HR-1) of the HIV-1 gp41 transmembrane envelope protein is aligned for viruses exhibiting different T-20 susceptibilities (**Table 6**). Highlighted amino acids represent mutations known to confer reduced susceptibility to T-20.

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